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Confirmation No.: 8485

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Date: December 5, 2008

Re: US Patent Application No. 09/051,843
Filed: June 29, 1998

CC:

"A NOVEL HAEMOPOIETIN
RECEPTOR AND GENETICS
SEQUENCES ENCODING SAME"

Our Docket: 11373

Art Unit: 1646

Confirmation No.: 8485

☐ Urgent ☐ For Review ☐ Please Comment ☐ Please Reply

FOR EXAMINER'S REVIEW AND DO NOT ENTER

Dear Examiner Howard:

Please see the attached Draft Amendment Under 37 C.F.R. §1.116.

Thank you.

Xiaochun Zhu, Ph.D.

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**RESPONSE UNDER 37 C.F.R.
§1.116 EXPEDITED PROCEDURE
EXAMINING GROUP 1646**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:	Tracy A. Willson, et al.	Examiner:	Zachary C. Howard
Serial No:	09/051,843	Art Unit:	1646
Filed:	June 29, 1998	Docket:	11373
For:	A NOVEL HAEMOPOIETIN RECEPTOR AND GENETIC SEQUENCES ENCODING SAME	Date:	<u>DRAFT</u>

Confirmation No.: 8485

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT UNDER 37 C.F.R. §1.116

Sir:

In response to the Final Action dated August 29, 2008 and in accordance with the provisions of 37 C.F.R. §1.116, Applicants respectfully request entry of the following amendment in the above-identified case.

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is being deposited with the United States Patent & Trademark Office via Electronic Filing through the United States Patent and Trademark Office e-business website on the date shown below.

Dated: **DRAFT**

Xiaochun Zhu

AMENDMENTS TO THE CLAIMS:

The following claim listing will replace all previous listings of the claims:

1. (Previously presented) An isolated nucleic acid molecule comprising a nucleotide sequence encoding an IL-13 receptor α -chain comprising the amino acid sequence set forth in SEQ ID NO:4.
2. (Currently amended) An isolated nucleic acid molecule comprising a nucleotide sequence encoding a derivative of an IL-13 receptor α -chain, wherein said receptor α -chain comprises the amino acid sequence as set forth in SEQ ID NO: 4, and wherein the derivative is an extracellular domain of the IL-13 receptor α -chain which comprises amino acids 28-[[342]]346 of SEQ ID NO: 4 or comprises an amino acid sequence having at least 95% identity with amino acids 28-342 of SEQ ID NO: 4, and wherein said derivative binds with IL-13.
- 3-6. (Cancelled)
7. (Currently amended) An isolated nucleic acid molecule comprising a sequence of nucleotides which encodes an IL-13 receptor α -chain, ~~said nucleic acid molecule comprising the nucleotide sequence as~~ wherein said sequence is set forth in SEQ ID NO: 3 or ~~comprising a nucleotide sequence which~~ hybridizes to the complement of the nucleotide sequence as set forth in SEQ ID NO: 3 under stringency conditions, and wherein said stringency conditions comprise hybridization in 5x SSC at 50°C and washing in 0.2x SSC at 50°C.
- 8-9. (Cancelled)
10. (Previously presented) An expression vector comprising a nucleic acid molecule according to any one of claims 1, 2 or 7, operably linked to a promoter which directs expression of said nucleic acid molecule in a host cell.
- 11-24. (Cancelled)
25. (Previously presented) A composition comprising a nucleic acid molecule according to any one of claims 1, 2 or 7, and a pharmaceutically acceptable carrier.

26-27. (Cancelled)

28. (Previously presented) A method of producing a recombinant polypeptide having at least two of the following characteristics:

- (i) comprises the amino acid sequence as set forth in SEQ ID NO:4;
- (ii) is encoded by the nucleotide sequence as set forth in SEQ ID NO:3;
- (iii) binds with IL-13 or its derivatives; and
- (iv) said polypeptide, when expressed in COS cells, has a molecular weight of from about 50,000 to about 70,000 daltons as determined by Western blot analysis,

said method comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express the nucleic acid molecule in said expression vector to produce a recombinant polypeptide and isolating said recombinant polypeptide.

29. (Previously presented) A method of producing a recombinant polypeptide having at least three of the following characteristics:

- (i) comprises the amino acid sequence as set forth in SEQ ID NO:4;
- (ii) is encoded by the nucleotide sequence as set forth in SEQ ID NO:3;
- (iii) binds with IL-13 or its derivatives;
- (iv) said polypeptide, when expressed in COS cells, has a molecular weight of from about 50,000 to about 70,000 daltons as determined by Western blot analysis;
- (v) comprises an amino acid sequence derived from IL-4 receptor α -chain; and
- (vi) is capable of interaction with IL-13 which is competitively inhibited by IL-4 in cells which express an IL-4 receptor α -chain,

said method comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express the nucleic acid molecule in said expression vector to produce a recombinant polypeptide and isolating said recombinant polypeptide.

30-36. (Cancelled)

37. (Previously presented) An isolated nucleic acid molecule comprising the nucleotide sequence as set forth in SEQ ID NO: 3.

38-42. (Cancelled)

43. (Currently amended) The isolated nucleic acid molecule of claim 2, encoding a polypeptide consisting of amino acids 28-~~[[342]]~~346 of SEQ ID NO: 4.

44. (Currently amended) ~~[[The]]~~An isolated nucleic acid molecule ~~of claim 1~~, encoding a polypeptide consisting of amino acids 28-426 of SEQ ID NO:4.

45-46. (Cancelled)

47. (Previously presented) A method of producing a recombinant polypeptide comprising culturing cells comprising the expression vector according to claim 10 for a time and under conditions sufficient to express a polypeptide encoded by said expression vector and isolating said recombinant polypeptide.

48. (Currently amended) The isolated nucleic acid sequence of claim ~~[[1]]~~2 wherein said sequence consists of nucleotides 142-~~[[1086]]~~1098 of SEQ ID NO: 3.

49. (Currently amended) ~~[[The]]~~An isolated nucleic acid ~~molecule sequence of claim 1~~ ~~wherein said sequence consists of~~ consisting of nucleotides 142-1338 of SEQ ID NO: 3.

50-52. (Cancelled)

53. (Previously presented) An isolated host cell transformed with the expression vector of claim 10.

54. (Previously presented) An isolated host cell which expresses a recombinant polypeptide encoded by a nucleic acid molecule according to any one of claims 1, 2 or 7.

REMARKS

In the Final Action dated August 29, 2008, claims 1, 2, 7, 10, 25, 28, 29, 37, 43, 44, 47-49, 53 and 54 are pending and under consideration. Claims 1 and 37 are allowed. Claims 44 and 49 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. Claims 2, 10, 25, 28, 29, 43, 47-48, 53 and 54 are rejected under 35 U.S.C. §112, first paragraph, for allegedly introducing new matter and failing to comply with the written description requirement. Claims 7 and 25 are rejected under 35 U.S.C. §102(b) as anticipated by NCBI Genbank EST Database Accession Number H57074.

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance, or at least in a better condition for appeal. Therefore, entry of the Response is warranted and favorable consideration of all pending claims is respectfully requested.

35 U.S.C. §112, Second Paragraph

Claims 44 and 49 are rejected as indefinite. Both claims 44 and 49 depend from claim 1. The Examiner indicates that as a result of the previous amendment to claim 1, the nucleic acids recited in claims 44 and 49 are no longer encompassed by the genus of claim 1.

In response, Applicants have rewritten claims 44 and 49 as independent claims. The rejection is overcome in light of these amendments, and withdrawal thereof is respectfully requested.

35 U.S.C. §112, First Paragraph

Claims 2, 10, 25, 28, 29, 43, 47-48, 53 and 54 are alleged to contain new matter and therefore fail to comply with the written description requirement. Specifically, the Examiner

states that the recitation of "the derivative comprises amino acids 28-342 of SEQ ID NO: 4", which appears in claim 2, introduces new matter for two reasons: (i) The specification does not teach a derivative of an IL-13 receptor α -chain that *consists of* residues 28-342 of SEQ ID NO: 4; and (ii) The specification does not teach derivatives of an IL-13 receptor α -chain that *comprises* residues 28-342 of SEQ ID NO: 4.

The Examiner is of the opinion that the specification does not teach that a derivative consisting of residues 28-342 of SEQ ID NO: 4 (human) is part of the claimed invention. The Examiner goes on to state that the specification does not even teach that a derivative consisting of the corresponding residues (27-340) of the mouse sequence (SEQ ID NO: 2) is part of the claimed invention. While the Examiner acknowledges that the specification teaches that a recombinant IL-13 α -chain may be in soluble form, the Examiner contends that the specification does not teach any specific soluble form except a single example of a murine soluble form (amino acids 27-344 of SEQ ID NO: 2).

Further, the Examiner takes the position that the single example of a murine soluble form (amino acids 27-344 of SEQ ID NO: 2) may provide support for a derivative consisting of the exact corresponding residues of the human sequence (Thr28-Thr346); however, it does not provide support for either a slightly shorter form of the murine (residues 27-340 of SEQ ID NO: 2) or the corresponding human (28-342 of SEQ ID NO: 4) sequences. According to the Examiner, there is nothing in the specification directing the skilled artisan to these slightly shorter sequences; and further, the specification does not contain any teachings indicating that a derivative consisting of the specific residues corresponding to the isolated extracellular domain of either protein is part of the invention.

Applicants respectfully submit that the written description requirement does not require *literal* recitation of the claimed subject matter in the specification. The proper legal standard concerning the written description requirement is whether the specification as originally filed conveys to those skilled in the art with reasonable clarity that the inventors had possession of the claimed invention at the time of filing. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-1564, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). In the present case, Example 6 on page 37 of the specification explicitly states that "the extracellular region of the protein contained an immunoglobulin like domain (amino acids 27-117), in addition to a typical haemopoietin receptor domain (amino acids 118-340)" (emphasis added). Further, as the Examiner has admitted, the specification clearly conveys to those skilled in the art that a soluble form of the IL-13R is part of the claimed invention. The Examiner has also noted himself that those in the art understand a soluble receptor to mean a receptor that has been rendered soluble by e.g., deleting all or a part of the transmembrane domain. In light of this common knowledge of those skilled in the art about a soluble receptor, and considering the entirety of the teaching in the specification, especially the specific reference to soluble forms and to the extracellular region of murine IL-13 receptor, those skilled in the art would have understood that a receptor that consists of the extracellular region (amino acids 27-340 of SEQ ID NO: 2) of murine IL-13R is part of the claimed invention. Those skilled in the art would then naturally deduce the human counterpart, i.e., amino acids 28-342 of SEQ ID NO: 4, as part of the claimed invention, based on the sequence alignment provided in Figure 7.

Moreover, Applicants respectfully submit that those skilled in the art would have understood from the specification that the invention would encompass soluble forms that contain additional amino acids beyond the extracellular domain. Again, as the Examiner has noted in the

Action, those in the art understand a soluble receptor to mean a receptor that has been rendered soluble by e.g., deleting *all or a part* of the transmembrane domain. Further, in the previous Action dated July 25, 2008, the Examiner agreed that variants that comprise the entire unaltered extracellular domain of human IL-13 α would probably retain binding to IL-13. In fact, as demonstrated in the present application, a soluble murine form (amino acids 27-344 of SEQ ID NO: 2), which includes four amino acids from the transmembrane segment in addition to the entire extracellular domain (amino acids 27-340), did bind to IL-13 (see page 40 of the specification).

Although Applicants disagree with the Examiner's reasoning, solely in an effort to advance prosecution, Applicants have amended claim 2 to revert to the recitation used previously, "wherein the derivative is an extracellular domain of the IL-13 receptor α -chain which comprises amino acids 28-346 of SEQ ID NO: 4". In addition, claims 43 and 48 have also amended to revert to the previous versions of amino acid and nucleotide positions. It is believed that the claims, as presently amended, are fully supported by the specification and do not introduce new matter.

In view of the foregoing, the rejection under 35 U.S.C. §112, first paragraph, is overcome. Withdrawal of the rejection is therefore respectfully requested.

35 U.S.C. §102(b)

Claims 7 and 25 are rejected under 35 U.S.C. §102(b) as allegedly anticipated NCBI Genbank EST Database Accession Number H57074. EST H57074 is a 154 nucleotide sequence that allegedly has 98.1% similarity to residues 469-623 of SEQ ID NO: 3, and would therefore hybridize to the complement of SEQ ID NO: 3, according to the Examiner.

The asserted EST has the following sequence:

```
aacctgagct acatgaagtg ttcttggctc cctggaagaa taccagtcctc
gacactaact atactctcta ctattggcac agaagcctgg naaaaattca
tcaatgtgaa aacatcttta gagaaggcca ataacttggt tgttcccttg
atct
```

Translation of this EST provides the following 51 amino acid peptide:

```
1 NLSYMKCSWL PGRIPVPTLT ILSTIGTEAW XKFINVKTSL EKANTLVVPL I 51
```

Alignment with the relevant portion of IL-13R α of SEQ ID NO:4 shows that while the first 13 amino acids are identical, only 2 of the remaining 38 amino acids are identical.

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1 NLSYMKCSWL PGRIPVPTLT ILSTIGTEAW XKFINVKTSL EKANTLVVPL I 51
137 NLSYMKCSWL PGRNTSPDTN YTLYYWHRSL EKIHCENIF REGQYFGCSF D 187
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Given its short length and low level of identity, Applicants respectfully submit that it is unlikely and it is improper for the Examiner to assume that this EST sequence would encode an IL-13R α -chain, as presently claimed. Therefore, Applicants respectfully submit that EST H57074 does not meet each and every element of the claimed invention. Accordingly, the rejection under 35 U.S.C. §102(b) is overcome, and withdrawal thereof is requested.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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